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10/589,290	08/11/2006	Susan Wimer-Mackin	LIGO-009/02US 306927-2062	5685
58249 7590 02/23/2010 COOLEY GODWARD KRONISH LLP ATTN: Patent Group Suite 1100 777 - 6th Street, NW WASHINGTON, DC 20001			EXAMINER DUFFY, PATRICIA ANN	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



### **RESPONSE TO AMENDMENT**

The amendment, response and affidavit filed 11-12-09 have been entered into the record. Claims 1-48, 50-53, 60 and 64-67 have been cancelled. Claims 49, 54-59, 61-63, and 68-79 are pending. Claims 49, 54-59, 61-63 and 78-79 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

#### ***Election/Restrictions***

This application contains claims 68-77 are drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### ***Rejections Withdrawn***

The objection to claims 64-67 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the cancellation of the claims. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims recite

The rejection of claims 49-58 and 64-67 under 35 U.S.C. 103(a) as being unpatentable over Schneerson et al (2006/0134143 published June 22, 2006 with priority to 60/476,598 filed on June 3, 2003) in view of Sigma Chemical Catalog 2002-2003, page 86, MPL+TDM emulsion is withdrawn in view of the amendment to the claims.

#### ***Rejections Maintained***

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims drawn to devices of this application. In

the instant case neither of the provisional filings provides for written description of nasal administration devices. Applicants pointing to paragraphs [077] and [078] do not teach the elements and conception of compositions comprising mucosal administration devices, specific adjuvants such as signaling transducer receptor of LPS, other positively charged polysaccharides, toll-like receptors in the now claimed combinations of mucosal adjuvants. The paragraphs to which applicants point only indicate powders.

Claims 49-59, 61-63, 78 and 79 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons made of record for claims 49-67 in the Office Action mailed 11-12-09.

Applicant's arguments have been carefully considered but are not persuasive. Applicant asserts that the claims do not recite epitopes or fragments. This is not persuasive because the specification defines anthrax peptide at paragraphs [046]-[049] of the specification and includes homologous variants and fragments and of any the full length native protective antigen (PA), lethal factor (LF), edema factor (EF), poly (gamma-D-glutamic acid (PGA) and BclA. Therefore, the recitation of protective antigen in the claim necessarily includes homologs and fragments. The specification necessarily includes in the definition epitopes and immunogenic fragments. Therefore, although, applicants teach the components of a dry powder formulation with the full length native protective antigen, the claims are not so limited in view of the definition in the specification. While not necessary to describe all dry powders, the art at the time of filing does not describe homologs, fragments or epitopes of protective antigen that can ameliorate or prevent at least one symptom of anthrax disease and does not describe how to make the dry powder of the working example. It merely describes the components of the dry powder. The specification does not teach how to make the dry powder formulations used in the specification. In the instant case, Applicants claim a dry powder vaccine, the specification

teaches that the mode of administration, dose of protective antigen and particular adjuvant or combinations of adjuvants materially affect the performance of the immunogen. Applicants are claiming in broad terms a dry powder mucosal vaccine but do not teach how to make such or do not reference any particular means in the art to arrive at such. In fact, in contrast to Applicant's argument, Applicants turned to a Pharmaceutical Service, who processed the combinations by unknown means containing perhaps unknown carriers, emulsifiers or agents to arrive at an unknown not reproducible dry powder composition that was administered intranasally to rabbits. Therefore, Applicants have not conveyed by means of written description that Applicants were in possession of the genus of formulation of dry powder vaccines as claimed. Applicants argue that the skill in the art knows how to make such with therapeutic proteins. This is not persuasive as there are currently available dry powder mucosal therapeutic vaccines comprising proteins available for use therefore Applicants assertion lacks evidence. The courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus (i.e. make and test to see if they lack the requisite activity) or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. Based on the lack of knowledge and predictability in this art, the lack of corresponding homologs and lack of any characterized sequenced protein homologs, lack of any characterized immunogenic fragment/epitope those of ordinary skill in the art would not conclude that the Applicant was in possession of the claimed genus of anthrax peptide variants or in possession of immunogenic fragments or epitopes that functioned to ameliorate or prevent at least one symptom of anthrax disease as claimed when formulated as a dry powder. Applicants' have no written description for any of these other desirable compounds are not enabled for such and that applicants' are not entitled for dominance of further patentable inventions by claims that are insufficiently supported by the specification (*In re Fisher*, 166 USPQ 18, CCPA (1970)). The courts have held "... in cases involving predictable factors, such as mechanical

Art Unit: 1645

or electrical elements, a single embodiment provide broad enablement in the sense that once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (*In re Fisher* 166 USPQ 18 (CCPA)). It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of the invention in order to constitute adequate enablement." *Genetech Inc. v. Novo Nordisk A/S* 42 USPQ2d 1001.

The rejection is maintained.

Claims 49-53, 57, 58, 61-63, and 79 stand rejected under 35 U.S.C. 102(a) as being anticipated by Miksztra et al (JID, 191:278-288, January 15, 2005 record on 1449) for reasons made of record in the Office Action mailed 11-12-09.

Applicant's arguments and declaration have been carefully considered but is not persuasive. Applicants argue that they are entitled to the earliest priority date and as such Miksztra et al is not prior art. This is not persuasive because priority of the provisional document is denied for reasons set forth above and the provisional documents are not in compliance with 35 USC 112, first paragraph as set forth directly above. Applicants also assert a declaration filed pursuant to 37 CFR 1.131 to attempt to establish that they were in possession of the invention before the critical date. The declaration is insufficient to obviate the reference because; the declaration does not establish an earlier reduction to practice in the United States, a NAFTA country or a WTO country. Second, the declaration does not teach as much as the reference because it does not show the species CpG. A reference or activity which discloses several species of a claimed genus can be overcome only by a showing that the applicant completed, prior to the date of the reference, all the species shown in the reference. MPEP 715.03I.B.

The rejection is maintained.

Claims 49-57, 61-63, 78 and 79 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schneerson et al (2006/0134143 published June 22, 2006 with priority to 60/476,598 filed on June 3, 2003) for reasons made of record in the Office Action mailed 11-12-09.

Applicant's arguments have been carefully considered but are not persuasive. Applicant argues that there is no suggestion in Schneerson to arrive at the claimed composition from all of the disclosed variables, this is not persuasive as applicants are specifically directed to the indicated disclosure and the claims. *In re Fine*, 837 F.2d 1071, 1075, 5U.S.P.Q.2d 1959 (Fed. Cir. 1988) states that under section 103 a *prima facie* case of obviousness can be established by showing some objective teaching in the prior art **or that knowledge generally available to one of ordinary skill in the art can lead the individual to combine the references**. See also *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Furthermore, the courts have held "The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See *In re Rosset*, 146 USPQ 183, 186 (CCPA 1965). "There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." *Motorola, Inc. v. Interdigital Tech. Corp.*, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997). Finally, an obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 2007 U.S. LEXIS 4745, 2007 WL 1237837, at \*12 (2007) ("The combination of familiar elements according

to known methods is likely to be obvious when it does no more than yield predictable results." ). This composition is merely a combination of known elements, yielding predictable results compositions comprising such and adjuvants were claimed and the adjuvants known to the art. Formulation as a dry powder for long term preservation and/or administration is routine in the pharmaceutical arts. Applicants argue that the dry powder compositions have superior properties as compared to a liquid formulation and reference Example 5. The first superior result allegedly provided for increased anti-PA IgG in serum, however, at page [0151-0152] all Applicant reports that all PA immunized rabbits survived challenge with a lethal inhalational dose of anthrax spores (inclusive of liquid formulation) and the lack of morbidity/aneorexia in the challenge groups was unrelated to anti-PA IgG levels. Therefore, there is no unexpected/superior result as it relates to the claim which merely requires that the composition ameliorate or prevent at last one symptom of anthrax disease. In this case both the animals administered the liquid or the powder performed the same as both the dry powder formulation and liquid formulation provided challenge protection. As such no superior results of the dry powder composition as opposed to the same administered in liquid form by the same route can be found.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the recombinant PA conjugated to a PGA peptide to the MPL adjuvant and formulate the immunogenic composition as a dry powder for use a dispensing means for intranasal or intrapulmonary administration in single or mulitdose formulations according to Schneerson et al because Schneerson et al teach that the recombinant PA conjugated to a PGA peptide can be so formulated and dispensed to the mucosal sites such as pulmonary, oral or nasal. The dose, unit or multi-unit formulation packaging along with single or multi-use devices are design choices well established in the art and the choice of unit dosing and multi or single use despensing devices are well within the skill of the pharmaceutical arts.

Claim 49-57, 61-63, 78 and 79 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schneerson et al (2006/0134143 published June 22, 2006 with priority to 60/476,598 filed on June 3, 2003) in view of Alpar et al , In: MVADS Conference 4<sup>th</sup>-6<sup>th</sup> of June 2003, Dublin, Republic of Ireland for reasons made of record in the Office Action mailed 11-12-09.

Applicant's arguments have been carefully considered but are not persuasive. Applicants argue that Schneerson does not teach multiple adjuvants and Alpar recites successful mucosal adjuvants and does not disclose dry powder formulations. Schneerson et al does not fail for reason set forth above and Alpar et al directs one to the specifically active mucosal adjuvants and discusses the advantages of adding chitosan to mucosal compositions and dry powder compositions are contemplated by the art. Alpar directs one to the combination for mucosal administration and provides for advantages.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Alpar provides specific mucosal adjuvants and enhancement of effects by chitosan and Schneerson provides for dry powder or liquid formulations.

### ***New Rejections Based on Amendment***

#### ***Claim Objections***

Claim 78 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to

cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 78 is apparently drawn to a liquid form. The liquid form fails to properly further limit the claim from which it depends (claim 49), since it is no longer a dry powder composition.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 78 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 78 depends from claim 49 which is drawn to a dry powder formulation. Claim 78 indicates an apparent process step indicating that the composition is reconstituted as a liquid. This limitation is unclear since how can a dry powder also be a liquid at the same time. What is applicant claiming a dry power or a liquid composition? Clarification is respectfully requested.

### ***Status of Claims***

Claims 49, 54-59, 61-63 and 78-79 stand rejected. Claims 68-77 are withdrawn from consideration.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 7:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisors, Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 10/589,290  
Art Unit: 1645

Page 11

/Patricia A. Duffy/  
Primary Examiner